

# SUBSTITUTE SEQUENCE LISTING

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<110> Anderson, John P.  
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Power, Michael  
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Wang, Shuwen  
McConlogue, Lisa  
Elan Pharmaceuticals, Inc.

<120> BETA-SECRETASE ENZYME COMPOSITIONS AND METHODS

<130> 015270-006430US

<140> US 09/471,669

<141> 1999-12-24

<150> US 60/114,408

<151> 1998-12-31

<150> US 60/119,571

<151> 1999-02-10

<150> US 60/139,172

<151> 1999-06-15

<160> 108

<170> PatentIn Ver. 2.1

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| ggcaccacag | acggcatccg  | gtgcccctg   | cgcagcggcc  | tgggggggag | ccccctgggg  | 120  |
| ctgaggctgc | cccgggagac  | cgacgaagag  | cccaggagag  | ccggccggag | gggcagcttt  | 180  |
| gtggagatgg | tggacaacct  | gaggggcaag  | tcggggcagg  | gctactacgt | ggagatgacc  | 240  |
| gtgggcagcc | cccgcgagac  | gtcacaacac  | ctgggtggata | caggcagcag | taactttgca  | 300  |
| gtgggtgctg | ccccccaccc  | cttcctgcat  | cgctactacc  | agaggcagct | gtccagcaca  | 360  |
| taccgggacc | tccggaaggg  | tgtgtatgtg  | ccctacaccc  | agggcaagtg | ggaaggggag  | 420  |
| ctgggcaccg | acctggttaag | catcccccat  | ggcccccaag  | tcactgtgcg | tgccaacatt  | 480  |
| gctgccatca | ctgaatcaga  | caagttcttc  | atcaacggct  | ccaactggga | aggcatcctg  | 540  |
| gggctggcct | atgctgagat  | tgccaggcct  | gacgactccc  | tggagccttt | ctttgactct  | 600  |
| ctggttaaag | agaccacagt  | tcccaacctc  | ttctccctgc  | agctttgtgg | tgctggcttc  | 660  |
| cccctcaacc | agtctgaagt  | gctggcctct  | gtcggaggga  | gcatgatcat | tggagggtatc | 720  |
| gaccactcgc | tgtacacagg  | cagtctctgg  | tatacaccca  | tccggcggga | gtggtattat  | 780  |
| gaggtgatca | ttgtgcgggt  | ggagatcaat  | ggacaggatc  | tgaaaatgga | ctgcaaggag  | 840  |
| tacaactatg | acaagagcat  | tgtggacagt  | ggcaccacca  | accttcggtt | gcccagaagaa | 900  |
| gtgtttgaag | ctgcagtcaa  | atccatcaag  | gcagcctcct  | ccacggagaa | gttccctgat  | 960  |
| ggtttctggc | taggagagca  | gctggtgtgc  | tggcaagcag  | gcaccacccc | ttggaacatt  | 1020 |
| ttcccagtc  | tctactcta   | cctaattgggt | gaggttacca  | accagtcctt | ccgcataccc  | 1080 |
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 245 250 255

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 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
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 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
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 405 410 415  
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
 420 425 430  
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 Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met Ala Ala  
 450 455 460  
 Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
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oligonucleotide primer derived from SEQ ID NO:2

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oligonucleotide primer derived from SEQ ID NO:2

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<212> DNA  
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<210> 18  
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<212> DNA

<213> Artificial Sequence

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<223> Description of Artificial Sequence: Degenerate  
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<212> DNA

<213> Artificial Sequence

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<210> 20

<211> 26

<212> DNA

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<211> 24

<212> DNA

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<210> 22

<211> 17

<212> DNA

<213> Artificial Sequence

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<223> n = a, c, g, or t.

<400> 22  
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gaygargagc cngaaga

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<210> 24  
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<210> 25  
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<211> 15  
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<210> 35  
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<223> Description of Artificial Sequence: Degenerate  
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<210> 39

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<212> DNA

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<223> Description of Artificial Sequence: Degenerate  
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<210> 40

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<213> Artificial Sequence

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<212> PRT  
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 35 40 45  
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
 50 55 60  
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
 65 70 75 80  
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
 85 90 95  
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
 100 105 110  
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
 115 120 125  
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
 130 135 140  
 Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
 145 150 155 160  
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro  
 165 170 175  
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
 180 185 190  
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
 195 200 205  
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 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
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96

d

Lys Phe Ala, Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
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 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala  
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 <223> Description of Artificial Sequence: Flag sequence

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 <212> PRT  
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Leu Gly Leu Arg Leu Pro Arg  
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 vector pCEK

<220>



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<400> 48

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 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
 20 25 30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
 165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285

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Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala

<210> 58  
 <211> 407  
 <212> PRT  
 <213> Homo sapiens

<400> 58  
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
 1 5 10 15  
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val  
 20 25 30  
 Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp  
 35 40 45  
 Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu  
 50 55 60  
 His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg  
 65 70 75 80  
 Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu  
 85 90 95  
 Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg  
 100 105 110  
 Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly  
 115 120 125  
 Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg  
 130 135 140

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Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr  
 145 150 155 160  
 His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro  
 165 170 175  
 Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile  
 180 185 190  
 Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro  
 195 200 205  
 Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile  
 210 215 220  
 Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys  
 225 230 235 240  
 Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val  
 245 250 255  
 Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys  
 260 265 270  
 Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala  
 275 280 285  
 Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met  
 290 295 300  
 Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln  
 305 310 315 320  
 Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr  
 325 330 335  
 Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val  
 340 345 350  
 Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile  
 355 360 365  
 Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala  
 370 375 380  
 Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr  
 385 390 395 400  
 Asn Ile Pro Gln Thr Asp Glu  
 405

<210> 59  
 <211> 452  
 <212> PRT  
 <213> Homo sapiens

<400> 59  
 Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
 1 5 10 15

Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
 20 25 30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160  
 Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
 165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335

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Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu  
 420 425 430  
 Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro  
 435 440 445  
 Gln Thr Asp Glu  
 450

<210> 60  
 <211> 420  
 <212> PRT  
 <213> Homo sapiens

<400> 60  
 Met Ala Gln Ala Leu Pro Trp Leu Leu Leu Trp Met Gly Ala Gly Val  
 1 5 10 15  
 Leu Pro Ala His Gly Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser  
 20 25 30  
 Gly Leu Gly Gly Ala Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp  
 35 40 45  
 Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val  
 50 55 60  
 Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr  
 65 70 75 80  
 Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser  
 85 90 95  
 Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr  
 100 105 110  
 Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val  
 115 120 125  
 Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp  
 130 135 140  
 Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile  
 145 150 155 160

Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp  
 165 170 175  
 Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp  
 180 185 190  
 Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Val Pro  
 195 200 205  
 Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln  
 210 215 220  
 Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile  
 225 230 235 240  
 Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg  
 245 250 255  
 Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln  
 260 265 270  
 Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val  
 275 280 285  
 Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala  
 290 295 300  
 Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp  
 305 310 315 320  
 Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr  
 325 330 335  
 Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val  
 340 345 350  
 Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg  
 355 360 365  
 Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala  
 370 375 380  
 Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu  
 385 390 395 400  
 Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala  
 405 410 415  
 Val Ser Ala Cys  
 420

<210> 61  
 <211> 7  
 <212> PRT  
 <213> Artificial Sequence

<220>  
 <223> Description of Artificial Sequence: Synthetic  
 peptide inhibitor

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d

<220>  
<221> MOD\_RES  
<222> (4)  
<223> Xaa = hydroxyethylene

<400> 61  
Glu Val Met Xaa Ala Glu Phe  
1 5

<210> 62  
<211> 26  
<212> PRT  
<213> Homo sapiens

<400> 62  
Leu Met Thr Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met  
1 5 10 15  
Leu Pro Leu Cys Leu Met Val Cys Gln Trp  
20 25

<210> 63  
<211> 33  
<212> PRT  
<213> Homo sapiens

<220>  
<223> P26-P4'sw peptide substrate

<400> 63  
Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
1 5 10 15  
Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Asp Ala Glu  
20 25 30

Phe

<210> 64  
<211> 29  
<212> PRT  
<213> Homo sapiens

<220>  
<223> P26-P1' peptide substrate with CGG linker

<400> 64  
Cys Gly Gly Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser Gly Leu  
1 5 10 15  
Thr Asn Ile Lys Thr Glu Glu Ile Ser Glu Val Asn Leu  
20 25

<210> 65  
<211> 427  
<212> PRT  
<213> Mus sp.

<220>

<223> pBS/MuImpain H#3 construct

<400> 65

Ile Asp Lys Leu Asp Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met  
1 5 10 15

Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met  
20 25 30

Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly  
35 40 45

Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg  
50 55 60

Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly  
65 70 75 80

Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr  
85 90 95

Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn  
100 105 110

Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn  
115 120 125

Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp  
130 135 140

Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile  
145 150 155 160

Pro Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn  
165 170 175

Gln Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly  
180 185 190

Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg  
195 200 205

Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly  
210 215 220

Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile  
225 230 235 240

Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu  
245 250 255

Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro  
260 265 270

Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr  
275 280 285

Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu  
290 295 300

Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu  
 305 310 315 320  
 Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe  
 325 330 335  
 Ala Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met  
 340 345 350  
 Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe  
 355 360 365  
 Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val  
 370 375 380  
 Glu Gly Pro Phe Val Thr Ala Asp Met Glu Asp Gly Tyr Asn Asn Arg  
 385 390 395 400  
 Ile Pro Ala Ala Arg Gly Ile His Phe Ser Gly Arg His Arg Gly Gly  
 405 410 415  
 Ala Pro Ile Arg Pro Ile Val Ser Arg Ile Asn  
 420 425

<210> 66  
 <211> 480  
 <212> PRT  
 <213> Homo sapiens

<400> 66  
 Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala  
 1 5 10 15  
 Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu  
 20 25 30  
 Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly  
 35 40 45  
 Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro  
 50 55 60  
 Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val  
 65 70 75 80  
 Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu  
 85 90 95  
 Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr  
 100 105 110  
 Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro  
 115 120 125  
 His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu  
 130 135 140

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser | Asn | Trp | Glu | Gly | Ile | Leu | Gly | 145 | 150 | 155 | 160 |
| Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro | Asp | Asp | Ser | Leu | Glu | Pro | Phe | 165 | 170 | 175 |     |
| Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His | Val | Pro | Asn | Leu | Phe | Ser | Leu | 180 | 185 | 190 |     |
| Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu | Asn | Gln | Ser | Glu | Val | Leu | Ala | 195 | 200 | 205 |     |
| Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly | Gly | Ile | Asp | His | Ser | Leu | Tyr | 210 | 215 | 220 |     |
| Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile | Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | 225 | 230 | 235 | 240 |
| Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn | Gly | Gln | Asp | Leu | Lys | Met | Asp | 245 | 250 | 255 |     |
| Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser | Ile | Val | Asp | Ser | Gly | Thr | Thr | 260 | 265 | 270 |     |
| Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe | Glu | Ala | Ala | Val | Lys | Ser | Ile | 275 | 280 | 285 |     |
| Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe | Pro | Asp | Gly | Phe | Trp | Leu | Gly | 290 | 295 | 300 |     |
| Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly | Thr | Thr | Pro | Trp | Asn | Ile | Phe | 305 | 310 | 315 | 320 |
| Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly | Glu | Val | Thr | Asn | Gln | Ser | Phe | 325 | 330 | 335 |     |
| Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr | Leu | Arg | Pro | Val | Glu | Asp | Val | 340 | 345 | 350 |     |
| Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr | Lys | Phe | Ala | Ile | Ser | Gln | Ser | Ser | 355 | 360 | 365 |     |
| Thr | Gly | Thr | Val | Met | Gly | Ala | Val | Ile | Met | Glu | Gly | Phe | Tyr | Val | Val | 370 | 375 | 380 |     |
| Phe | Asp | Arg | Ala | Arg | Lys | Arg | Ile | Gly | Phe | Ala | Val | Ser | Ala | Cys | His | 385 | 390 | 395 | 400 |
| Val | His | Asp | Glu | Phe | Arg | Thr | Ala | Ala | Val | Glu | Gly | Pro | Phe | Val | Thr | 405 | 410 | 415 |     |
| Leu | Asp | Met | Glu | Asp | Cys | Gly | Tyr | Asn | Ile | Pro | Gln | Thr | Asp | Glu | Ser | 420 | 425 | 430 |     |
| Thr | Leu | Met | Thr | Ile | Ala | Tyr | Val | Met | Ala | Ala | Ile | Cys | Ala | Leu | Phe | 435 | 440 | 445 |     |
| Met | Leu | Pro | Leu | Cys | Leu | Met | Val | Cys | Gln | Trp | Arg | Cys | Leu | Arg | Cys | 450 | 455 | 460 |     |



Leu Arg Gln Gln His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys  
 465 470 475 480

<210> 67  
 <211> 444  
 <212> PRT  
 <213> Homo sapiens

<400> 67  
 Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln  
 1 5 10 15  
 Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn  
 20 25 30  
 Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro  
 35 40 45  
 His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr  
 50 55 60  
 Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
 65 70 75 80  
 Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
 85 90 95  
 Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe  
 100 105 110  
 Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala  
 115 120 125  
 Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu  
 130 135 140  
 Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly  
 145 150 155 160  
 Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly  
 165 170 175  
 Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu  
 180 185 190  
 Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val  
 195 200 205  
 Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr  
 210 215 220  
 Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu  
 225 230 235 240  
 Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser  
 245 250 255

Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val  
 260 265 270  
 Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser  
 275 280 285  
 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile  
 290 295 300  
 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln  
 305 310 315 320  
 Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val  
 325 330 335  
 Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala  
 340 345 350  
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu  
 355 360 365  
 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
 370 375 380  
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr  
 385 390 395 400  
 Ile Ala Tyr Val Met Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu  
 405 410 415  
 Cys Leu Met Val Cys Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln  
 420 425 430  
 His Asp Asp Phe Ala Asp Asp Ile Ser Leu Leu Lys  
 435 440

<210> 68  
 <211> 395  
 <212> PRT  
 <213> Homo sapiens

<400> 68  
 Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln  
 1 5 10 15  
 Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn  
 20 25 30  
 Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro  
 35 40 45  
 His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr  
 50 55 60  
 Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp  
 65 70 75 80  
 Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn  
 85 90 95

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d

Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe  
 100 105 110  
 Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala  
 115 120 125  
 Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu  
 130 135 140  
 Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly  
 145 150 155 160  
 Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly  
 165 170 175  
 Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu  
 180 185 190  
 Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val  
 195 200 205  
 Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr  
 210 215 220  
 Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu  
 225 230 235 240  
 Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser  
 245 250 255  
 Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val  
 260 265 270  
 Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser  
 275 280 285  
 Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile  
 290 295 300  
 Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln  
 305 310 315 320  
 Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val  
 325 330 335  
 Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala  
 340 345 350  
 Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu  
 355 360 365  
 Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu  
 370 375 380  
 Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu  
 385 390 395

<210> 69  
 <211> 439  
 <212> PRT

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d

<213> \*Homo sapiens

<400> 69

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Met | Val | Asp | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | Glu |  |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |  |
| Met | Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | Thr |  |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |  |
| Gly | Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | His |  |
|     |     |     | 35  |     |     |     | 40  |     |     |     |     | 45  |     |     |     |  |
| Arg | Tyr | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | Lys |  |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |  |
| Gly | Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | Gly |  |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |  |
| Thr | Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | Ala |  |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     |     | 95  |  |
| Asn | Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser |  |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |  |
| Asn | Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro |  |
|     |     | 115 |     |     |     | 120 |     |     |     |     |     | 125 |     |     |     |  |
| Asp | Asp | Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His |  |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |
| Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu |  |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |
| Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly |  |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |  |
| Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile |  |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     |     | 190 |     |  |
| Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn |  |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |
| Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser |  |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |
| Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe |  |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly |  |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |  |
| Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly |  |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |
| Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr |  |
|     |     | 290 |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |

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Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys  
 305 310 315 320  
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
 325 330 335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
 340 345 350  
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala  
 355 360 365  
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn  
 370 375 380  
 Ile Pro Gln Thr Asp Glu Ser Thr Leu Met Thr Ile Ala Tyr Val Met  
 385 390 395 400  
 Ala Ala Ile Cys Ala Leu Phe Met Leu Pro Leu Cys Leu Met Val Cys  
 405 410 415  
 Gln Trp Arg Cys Leu Arg Cys Leu Arg Gln Gln His Asp Asp Phe Ala  
 420 425 430  
 Asp Asp Ile Ser Leu Leu Lys  
 435

<210> 70  
 <211> 390  
 <212> PRT  
 <213> Homo sapiens

<400> 70  
 Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
 1 5 10 15  
 Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
 20 25 30  
 Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
 35 40 45  
 Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
 50 55 60  
 Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
 65 70 75 80  
 Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
 85 90 95  
 Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
 100 105 110  
 Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
 115 120 125  
 Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
 130 135 140

Val•Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
 145 150 155 160  
 Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
 165 170 175  
 Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
 180 185 190  
 Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
 195 200 205  
 Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser  
 210 215 220  
 Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe  
 225 230 235 240  
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe  
 245 250 255  
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly  
 260 265 270  
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly  
 275 280 285  
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr  
 290 295 300  
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys  
 305 310 315 320  
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
 325 330 335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
 340 345 350  
 Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala  
 355 360 365  
 Val Glu Gly Pro Phe Val Thr Leu Asp Met Glu Asp Cys Gly Tyr Asn  
 370 375 380  
 Ile Pro Gln Thr Asp Glu  
 385 390

<210> 71  
 <211> 374  
 <212> PRT  
 <213> Homo sapiens

<400> 71  
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
 1 5 10 15  
 Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val  
 20 25 30

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| Glu | Met | Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp |  |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |  |
| Thr | Gly | Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu |  |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |  |
| His | Arg | Tyr | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg |  |
|     | 65  |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |  |
| Lys | Gly | Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu |  |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |  |
| Gly | Thr | Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg |  |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |  |
| Ala | Asn | Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly |  |
|     |     | 115 |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |  |
| Ser | Asn | Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg |  |
|     | 130 |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |  |
| Pro | Asp | Asp | Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr |  |
|     | 145 |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |  |
| His | Val | Pro | Asn | Leu | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro |  |
|     |     |     |     | 165 |     |     |     | 170 |     |     |     |     |     | 175 |     |  |
| Leu | Asn | Gln | Ser | Glu | Val | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile |  |
|     |     |     | 180 |     |     |     |     | 185 |     |     |     |     | 190 |     |     |  |
| Gly | Gly | Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro |  |
|     |     | 195 |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |  |
| Ile | Arg | Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile |  |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |  |
| Asn | Gly | Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys |  |
|     | 225 |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |  |
| Ser | Ile | Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val |  |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |  |
| Phe | Glu | Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys |  |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |  |
| Phe | Pro | Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala |  |
|     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |  |
| Gly | Thr | Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met |  |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |  |
| Gly | Glu | Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln |  |
|     | 305 |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |  |
| Tyr | Leu | Arg | Pro | Val | Glu | Asp | Val | Ala | Thr | Ser | Gln | Asp | Asp | Cys | Tyr |  |
|     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |     | 335 |     |  |
| Lys | Phe | Ala | Ile | Ser | Gln | Ser | Ser | Thr | Gly | Thr | Val | Met | Gly | Ala | Val |  |
|     |     |     | 340 |     |     |     |     | 345 |     |     |     |     | 350 |     |     |  |

Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile  
355 360 365

Gly Phe Ala Val Ser Ala  
370

<210> 72  
<211> 14  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: P10-P4'staD-V  
peptide inhibitor

<220>  
<221> MOD\_RES  
<222> (10)  
<223> Xaa is statine moiety

<400> 72  
Lys Thr Glu Glu Ile Ser Glu Val Asn Xaa Val Ala Glu Phe  
1 5 10

<210> 73  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: P4-P4'staD-V  
peptide inhibitor

<220>  
<221> MOD\_RES  
<222> (5)  
<223> Xaa is statine moiety

<400> 73  
Ser Glu Val Asn Xaa Val Ala Glu Phe  
1 5

<210> 74  
<211> 431  
<212> PRT  
<213> Homo sapiens

<400> 74  
Thr Gln His Gly Ile Arg Leu Pro Leu Arg Ser Gly Leu Gly Gly Ala  
1 5 10 15

Pro Leu Gly Leu Arg Leu Pro Arg Glu Thr Asp Glu Glu Pro Glu Glu  
20 25 30

Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp Asn Leu Arg Gly  
35 40 45



Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val Gly Ser Pro Pro  
 50 55 60  
 Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser Asn Phe Ala Val  
 65 70 75 80  
 Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu  
 85 90 95  
 Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr  
 100 105 110  
 Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu Val Ser Ile Pro  
 115 120 125  
 His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala Ala Ile Thr Glu  
 130 135 140  
 Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly  
 145 150 155 160  
 Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe  
 165 170 175  
 Phe Asp Ser Leu Val Lys Gln Thr His Val Pro Asn Leu Phe Ser Leu  
 180 185 190  
 Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Ser Glu Val Leu Ala  
 195 200 205  
 Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp His Ser Leu Tyr  
 210 215 220  
 Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu  
 225 230 235 240  
 Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp Leu Lys Met Asp  
 245 250 255  
 Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp Ser Gly Thr Thr  
 260 265 270  
 Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala Val Lys Ser Ile  
 275 280 285  
 Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly  
 290 295 300  
 Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe  
 305 310 315 320  
 Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr Asn Gln Ser Phe  
 325 330 335  
 Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro Val Glu Asp Val  
 340 345 350  
 Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Ile Ser Gln Ser Ser  
 355 360 365

Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly Phe Tyr Val Val  
370 375 380

Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val Ser Ala Cys His  
385 390 395 400

Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly Pro Phe Val Thr  
405 410 415

Leu Asp Met Glu Asp Cys Gly Tyr Asn Ile Pro Gln Thr Asp Glu  
420 425 430

<210> 75

<211> 361

<212> PRT

<213> Homo sapiens

<400> 75

Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu  
1 5 10 15

Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr  
20 25 30

Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His  
35 40 45

Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys  
50 55 60

Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly  
65 70 75 80

Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala  
85 90 95

Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser  
100 105 110

Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro  
115 120 125

Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His  
130 135 140

Val Pro Asn Leu Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu  
145 150 155 160

Asn Gln Ser Glu Val Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly  
165 170 175

Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile  
180 185 190

Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn  
195 200 205

Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser  
210 215 220

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Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe  
 225 230 235 240  
 Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe  
 245 250 255  
 Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly  
 260 265 270  
 Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly  
 275 280 285  
 Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr  
 290 295 300  
 Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys  
 305 310 315 320  
 Phe Ala Ile Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile  
 325 330 335  
 Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly  
 340 345 350  
 Phe Ala Val Ser Ala Cys His Val His  
 355 360

<210> 76  
 <211> 63  
 <212> DNA  
 <213> Homo sapiens

<220>  
 <221> misc\_feature  
 <222> (1)..(63)  
 <223> n = a, c, g, or t.

<400> 76  
 garacngayg argarccnga rgarccnggn mgnmgnggnw snttygtnga ratggtngay 60  
 aay 63

<210> 77  
 <211> 21  
 <212> PRT  
 <213> Homo sapiens

<400> 77  
 Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
 1 5 10 15

Glu Met Val Asp Asn  
 20

<210> 78  
 <211> 7  
 <212> PRT  
 <213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Peptide  
inhibitor P3-P4' XD-V

<220>  
<221> MOD\_RES  
<222> (3)  
<223> Xaa is hydroxyethylene or statine

<400> 78  
Val Met Xaa Val Ala Glu Phe  
1 5

<210> 79  
<211> 11  
<212> PRT  
<213> Homo sapiens

<400> 79  
Pro Glu Glu Pro Gly Arg Arg Gly Ser Phe Val  
1 5 10

<210> 80  
<211> 419  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Nucleotide  
insert in vector pCF

<400> 80  
ctgttgggct cgcggttgag gacaaactct tcgcggtctt tccagtactc ttggatcgga 60  
aaccgctcgg cctccgaacg gtactccgcc accgagggac ctgagcgagt ccgcatcgac 120  
cggatcggaa aacctctcga ctgttggggg gagtactccc tctcaaaagc gggcatgact 180  
tctgcgctaa gattgtcagt ttccaaaaac gaggaggatt tgatattcac ctggcccgcg 240  
gtgatgcctt tgagggtggc cgcgtccatc tggtcagaaa agacaatctt tttgttgtca 300  
agcttgaggt gtggcaggct tgagatctgg ccatacactt gaggtagaat gacatccact 360  
ttgcctttct ctccacaggt gtccactccc aggtccaact gcaggtcgac tctagaccc 419

<210> 81  
<211> 8  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Peptide  
inhibitor P4-P4' XD-V

<220>  
<221> MOD\_RES  
<222> (4)  
<223> Xaa is hydroxyethylene or statine.

<400> 81  
Glu Val Met Xaa Val Ala Glu Phe  
1 5

<210> 82  
<211> 9  
<212> PRT  
<213> Homo sapiens

<400> 82  
Ser Glu Val Lys Met Asp Ala Glu Phe  
1 5

<210> 83  
<211> 9  
<212> PRT  
<213> Homo sapiens

<220>  
<223> APP fragment P5-P4' wt

<400> 83  
Ser Glu Val Asn Leu Asp Ala Glu Phe  
1 5

<210> 84  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: APP fragment

<400> 84  
Ser Glu Val Lys Leu Asp Ala Glu Phe  
1 5

<210> 85  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: APP fragment

<400> 85  
Ser Glu Val Lys Phe Asp Ala Glu Phe  
1 5

<210> 86  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: APP fragment

<400> 86  
Ser Glu Val Asn Phe Asp Ala Glu Phe  
1 5

<210> 87  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Description of Artificial Sequence: APP fragment  
  
 <400> 87  
 Ser Glu Val Lys Met Ala Ala Glu Phe  
   1                  5  
  
 <210> 88  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Description of Artificial Sequence: APP fragment  
  
 <400> 88  
 Ser Glu Val Asn Leu Ala Ala Glu Phe  
   1                  5  
  
 <210> 89  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Description of Artificial Sequence: APP fragment  
  
 <400> 89  
 Ser Glu Val Lys Leu Ala Ala Glu Phe  
   1                  5  
  
 <210> 90  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Description of Artificial Sequence: APP fragment  
  
 <400> 90  
 Ser Glu Val Lys Met Leu Ala Glu Phe  
   1                  5  
  
 <210> 91  
 <211> 9  
 <212> PRT  
 <213> Artificial Sequence  
  
 <220>  
 <223> Description of Artificial Sequence: APP fragment

<400> 91  
Ser Glu Val Asn Leu Leu Ala Glu Phe  
1 5

<210> 92  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: APP fragment

<400> 92  
Ser Glu Val Lys Leu Leu Ala Glu Phe  
1 5

<210> 93  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: APP fragment

<400> 93  
Ser Glu Val Lys Phe Ala Ala Glu Phe  
1 5

<210> 94  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: APP fragment

<400> 94  
Ser Glu Val Asn Phe Ala Ala Glu Phe  
1 5

<210> 95  
<211> 9  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: APP fragment

<400> 95  
Ser Glu Val Lys Phe Leu Ala Glu Phe  
1 5

<210> 96  
<211> 9  
<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: APP fragment

<400> 96

Ser Glu Val Asn Phe Leu Ala Glu Phe

1

5

<210> 97

<211> 14

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: APP-derived  
fragment P10-P4' (D-V)

<400> 97

Lys Thr Glu Glu Ile Ser Glu Val Asn Leu Val Ala Glu Phe

1

5

10

<210> 98

<211> 35

<212> DNA

<213> Homo sapiens

<400> 98

cccgaagagc ccggccggag gggcagcttt gtcga

35

<210> 99

<211> 11

<212> PRT

<213> Homo sapiens

<400> 99

Glu Thr Asp Glu Glu Pro Glu Glu Pro Gly Arg

1

5

10

<210> 100

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: N terminal  
peptide of beta-secretase secreted from 293T cells

<400> 100

Thr Gln His Gly Ile Arg Leu Pro Leu Arg

1

5

10

<210> 101

<211> 9

<212> PRT

<213> Artificial Sequence



<220>

<223> Description of Artificial Sequence: N-terminal  
peptide sequence of beta-secretase secreted from  
293T cells

<400> 101

Met Val Asp Asn Leu Arg Gly Lys Ser  
1 5

<210> 102

<211> 10

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: N terminal  
peptide sequence of a form of beta-secretase  
isolated from recombinant CosA2 cells.

<400> 102

Gly Ser Phe Val Glu Met Val Asp Asn Leu  
1 5 10

<210> 103

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Beta-secretase  
cleavage site in wild-type APP sequence

<400> 103

Val Lys Met Asp  
1

<210> 104

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Beta-secretase  
cleavage site in APP bearing Swedish mutation

<400> 104

Val Asn Leu Asp  
1

<210> 105

<211> 408

<212> PRT

<213> Mus sp.

<220>

<223> pBS/MuImpain E17 #11 construct

131

d

<400> 105

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Ser | Ile | Ser | Leu | Ile | Glu | Pro | Gly | Arg | Arg | Gly | Ser | Phe | Val | Glu | Met |
| 1   |     |     |     | 5   |     |     |     |     | 10  |     |     |     |     | 15  |     |
| Val | Asn | Asn | Leu | Arg | Gly | Lys | Ser | Gly | Gln | Gly | Tyr | Tyr | Val | Glu | Met |
|     |     |     | 20  |     |     |     |     | 25  |     |     |     |     | 30  |     |     |
| Thr | Val | Gly | Ser | Pro | Pro | Gln | Thr | Leu | Asn | Ile | Leu | Val | Asp | Thr | Gly |
|     |     | 35  |     |     |     |     | 40  |     |     |     |     | 45  |     |     |     |
| Ser | Ser | Asn | Phe | Ala | Val | Gly | Ala | Ala | Pro | His | Pro | Phe | Leu | His | Arg |
|     | 50  |     |     |     |     | 55  |     |     |     |     | 60  |     |     |     |     |
| Tyr | Tyr | Gln | Arg | Gln | Leu | Ser | Ser | Thr | Tyr | Arg | Asp | Leu | Arg | Lys | Gly |
| 65  |     |     |     |     | 70  |     |     |     |     | 75  |     |     |     |     | 80  |
| Val | Tyr | Val | Pro | Tyr | Thr | Gln | Gly | Lys | Trp | Glu | Gly | Glu | Leu | Gly | Thr |
|     |     |     |     | 85  |     |     |     |     | 90  |     |     |     |     | 95  |     |
| Asp | Leu | Val | Ser | Ile | Pro | His | Gly | Pro | Asn | Val | Thr | Val | Arg | Ala | Asn |
|     |     |     | 100 |     |     |     |     | 105 |     |     |     |     | 110 |     |     |
| Ile | Ala | Ala | Ile | Thr | Glu | Ser | Asp | Lys | Phe | Phe | Ile | Asn | Gly | Ser | Asn |
|     | 115 |     |     |     |     |     | 120 |     |     |     |     | 125 |     |     |     |
| Trp | Glu | Gly | Ile | Leu | Gly | Leu | Ala | Tyr | Ala | Glu | Ile | Ala | Arg | Pro | Asp |
| 130 |     |     |     |     |     | 135 |     |     |     |     | 140 |     |     |     |     |
| Asp | Ser | Leu | Glu | Pro | Phe | Phe | Asp | Ser | Leu | Val | Lys | Gln | Thr | His | Ile |
| 145 |     |     |     |     | 150 |     |     |     |     | 155 |     |     |     |     | 160 |
| Pro | Asn | Ile | Phe | Ser | Leu | Gln | Leu | Cys | Gly | Ala | Gly | Phe | Pro | Leu | Asn |
|     |     |     |     | 165 |     |     |     |     | 170 |     |     |     |     | 175 |     |
| Gln | Thr | Glu | Ala | Leu | Ala | Ser | Val | Gly | Gly | Ser | Met | Ile | Ile | Gly | Gly |
|     |     | 180 |     |     |     |     |     | 185 |     |     |     |     | 190 |     |     |
| Ile | Asp | His | Ser | Leu | Tyr | Thr | Gly | Ser | Leu | Trp | Tyr | Thr | Pro | Ile | Arg |
|     | 195 |     |     |     |     |     | 200 |     |     |     |     | 205 |     |     |     |
| Arg | Glu | Trp | Tyr | Tyr | Glu | Val | Ile | Ile | Val | Arg | Val | Glu | Ile | Asn | Gly |
|     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |     |     |     |
| Gln | Asp | Leu | Lys | Met | Asp | Cys | Lys | Glu | Tyr | Asn | Tyr | Asp | Lys | Ser | Ile |
| 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |     |     | 240 |
| Val | Asp | Ser | Gly | Thr | Thr | Asn | Leu | Arg | Leu | Pro | Lys | Lys | Val | Phe | Glu |
|     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |     | 255 |     |
| Ala | Ala | Val | Lys | Ser | Ile | Lys | Ala | Ala | Ser | Ser | Thr | Glu | Lys | Phe | Pro |
|     |     |     | 260 |     |     |     |     | 265 |     |     |     |     | 270 |     |     |
| Asp | Gly | Phe | Trp | Leu | Gly | Glu | Gln | Leu | Val | Cys | Trp | Gln | Ala | Gly | Thr |
|     | 275 |     |     |     |     |     | 280 |     |     |     |     | 285 |     |     |     |
| Thr | Pro | Trp | Asn | Ile | Phe | Pro | Val | Ile | Ser | Leu | Tyr | Leu | Met | Gly | Glu |
|     | 290 |     |     |     |     | 295 |     |     |     |     | 300 |     |     |     |     |
| Val | Thr | Asn | Gln | Ser | Phe | Arg | Ile | Thr | Ile | Leu | Pro | Gln | Gln | Tyr | Leu |
| 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |     |     | 320 |

Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe  
 325 330 335  
 Ala Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met  
 340 345 350  
 Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe  
 355 360 365  
 Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val  
 370 375 380  
 Glu Gly Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Asn  
 385 390 395 400  
 Arg Ile Pro Ala Ala Arg Gly Ile  
 405

<210> 106  
 <211> 401  
 <212> PRT  
 <213> Mus sp.

<220>  
 <223> pBS/MuImpain E17 #14 construct

<400> 106  
 Lys Leu Asp Glu Pro Gly Arg Arg Gly Ser Phe Val Glu Met Val Asp  
 1 5 10 15  
 Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr Tyr Val Glu Met Thr Val  
 20 25 30  
 Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu Val Asp Thr Gly Ser Ser  
 35 40 45  
 Asn Phe Ala Val Gly Ala Ala Pro His Pro Phe Leu His Arg Tyr Tyr  
 50 55 60  
 Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp Leu Arg Lys Gly Val Tyr  
 65 70 75 80  
 Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly Glu Leu Gly Thr Asp Leu  
 85 90 95  
 Val Ser Ile Pro His Gly Pro Asn Val Thr Val Arg Ala Asn Ile Ala  
 100 105 110  
 Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile Asn Gly Ser Asn Trp Glu  
 115 120 125  
 Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile Ala Arg Pro Asp Asp Ser  
 130 135 140  
 Leu Glu Pro Phe Phe Asp Ser Leu Val Lys Gln Thr His Ile Pro Asn  
 145 150 155 160  
 Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly Phe Pro Leu Asn Gln Thr  
 165 170 175

Glu Ala Leu Ala Ser Val Gly Gly Ser Met Ile Ile Gly Gly Ile Asp  
 180 185 190  
 His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr Thr Pro Ile Arg Arg Glu  
 195 200 205  
 Trp Tyr Tyr Glu Val Ile Ile Val Arg Val Glu Ile Asn Gly Gln Asp  
 210 215 220  
 Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr Asp Lys Ser Ile Val Asp  
 225 230 235 240  
 Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys Lys Val Phe Glu Ala Ala  
 245 250 255  
 Val Lys Ser Ile Lys Ala Ala Ser Ser Thr Glu Lys Phe Pro Asp Gly  
 260 265 270  
 Phe Trp Leu Gly Glu Gln Leu Val Cys Trp Gln Ala Gly Thr Thr Pro  
 275 280 285  
 Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr Leu Met Gly Glu Val Thr  
 290 295 300  
 Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro Gln Gln Tyr Leu Arg Pro  
 305 310 315 320  
 Val Glu Asp Val Ala Thr Ser Gln Asp Asp Cys Tyr Lys Phe Ala Val  
 325 330 335  
 Ser Gln Ser Ser Thr Gly Thr Val Met Gly Ala Val Ile Met Glu Gly  
 340 345 350  
 Phe Tyr Val Val Phe Asp Arg Ala Arg Lys Arg Ile Gly Phe Ala Val  
 355 360 365  
 Ser Ala Cys His Val His Asp Glu Phe Arg Thr Ala Ala Val Glu Gly  
 370 375 380  
 Pro Phe Val Thr Ala Asp Met Glu Asp Cys Gly Tyr Asn Asn Arg Ile  
 385 390 395 400  
 Gln

<210> 107

<211> 231

<212> PRT

<213> Mus sp.

<220>

<223> pBS/MuImpain E17 Brain #17 construct

<400> 107

Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr  
 1 5 10 15

Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu  
 20 25 30

Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro  
 35 40 45  
 Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp  
 50 55 60  
 Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly  
 65 70 75 80  
 Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr  
 85 90 95  
 Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Val  
 100 105 110  
 Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile  
 115 120 125  
 Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys  
 130 135 140  
 Gln Thr His Ile Pro Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly  
 145 150 155 160  
 Phe Pro Leu Asn Gln Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met  
 165 170 175  
 Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr  
 180 185 190  
 Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val  
 195 200 205  
 Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr  
 210 215 220  
 Asp Lys Ser Ile Val Asp Ser  
 225 230

<210> 108  
 <211> 380  
 <212> PRT  
 <213> Mus sp.

<220>  
 <223> pBS/MuImpain E17 Brain#15 construct

<400> 108  
 Phe Val Glu Met Val Asp Asn Leu Arg Gly Lys Ser Gly Gln Gly Tyr  
 1 5 10 15  
 Tyr Val Glu Met Thr Val Gly Ser Pro Pro Gln Thr Leu Asn Ile Leu  
 20 25 30  
 Val Asp Thr Gly Ser Ser Asn Phe Ala Val Gly Ala Ala Pro His Pro  
 35 40 45  
 Phe Leu His Arg Tyr Tyr Gln Arg Gln Leu Ser Ser Thr Tyr Arg Asp  
 50 55 60

125

d

Leu Arg Lys Gly Val Tyr Val Pro Tyr Thr Gln Gly Lys Trp Glu Gly  
 65 70 75 80  
 Glu Leu Gly Thr Asp Leu Val Ser Ile Pro His Gly Pro Asn Val Thr  
 85 90 95  
 Val Arg Ala Asn Ile Ala Ala Ile Thr Glu Ser Asp Lys Phe Phe Ile  
 100 105 110  
 Asn Gly Ser Asn Trp Glu Gly Ile Leu Gly Leu Ala Tyr Ala Glu Ile  
 115 120 125  
 Ala Arg Pro Asp Asp Ser Leu Glu Pro Phe Phe Asp Ser Leu Val Lys  
 130 135 140  
 Gln Thr His Ile Pro Asn Ile Phe Ser Leu Gln Leu Cys Gly Ala Gly  
 145 150 155 160  
 Phe Pro Leu Asn Gln Thr Glu Ala Leu Ala Ser Val Gly Gly Ser Met  
 165 170 175  
 Ile Ile Gly Gly Ile Asp His Ser Leu Tyr Thr Gly Ser Leu Trp Tyr  
 180 185 190  
 Thr Pro Ile Arg Arg Glu Trp Tyr Tyr Glu Val Ile Ile Val Arg Val  
 195 200 205  
 Glu Ile Asn Gly Gln Asp Leu Lys Met Asp Cys Lys Glu Tyr Asn Tyr  
 210 215 220  
 Asp Lys Ser Ile Val Asp Ser Gly Thr Thr Asn Leu Arg Leu Pro Lys  
 225 230 235 240  
 Lys Val Phe Glu Ala Ala Val Lys Ser Ile Lys Ala Ala Ser Ser Thr  
 245 250 255  
 Glu Lys Phe Pro Asp Gly Phe Trp Leu Gly Glu Gln Leu Val Cys Trp  
 260 265 270  
 Gln Ala Gly Thr Thr Pro Trp Asn Ile Phe Pro Val Ile Ser Leu Tyr  
 275 280 285  
 Leu Met Gly Glu Val Thr Asn Gln Ser Phe Arg Ile Thr Ile Leu Pro  
 290 295 300  
 Gln Gln Tyr Leu Arg Pro Val Glu Asp Val Ala Thr Ser Gln Asp Asp  
 305 310 315 320  
 Cys Tyr Lys Phe Ala Val Ser Gln Ser Ser Thr Gly Thr Val Met Gly  
 325 330 335  
 Ala Val Ile Met Glu Gly Phe Tyr Val Val Phe Asp Arg Ala Arg Lys  
 340 345 350  
 Arg Ile Gly Phe Ala Val Ser Ala Cys His Val His Asp Glu Phe Arg  
 355 360 365  
 Thr Ala Ala Val Glu Gly Pro Phe Val Thr Ala Asp  
 370 375 380